

Rare Polyps Without Spots & Vice Versa

This morning I am going to tell you about the clinical syndrome in which I have been much interested for several years. The components of the syndrome are intestinal polyposis and melanin spots of the buccal mucosa, lips and digits. I will tell you about the five cases I have studied myself and about five cases of Dr. Leghers with whom I have pooled case material. You will see that the polyposis of this syndrome occurs characteristically in the small intestine although the entire length of the G.I. tract may be involved. Furthermore there is considerable variability in the extent of the melanin spotting, although spotting of the mouth particularly the buccal mucosa is a sine qua non of the pigmentary portion of the syndrome. Finally you will see that although sporadic cases occur there is ample evidence that this syndrome is hereditary being transmitted as a Mendelian dominant.

(Case 1) I saw my first case of this syndrome in 1946. The patient, a mulatto boy from here in Baltimore was 15 years old at that time. The patient had suffered all his life from complications of intestinal polyposis. At the age of 8 months he began to have repeated prolapse due to polyps and this continued off and on until the age of 4 when the last rectal polyp was finally removed. But at the age of six he began to have attacks of severe periumbilical pain almost monthly. These tended to come on after eating a particularly heavy meal and were frequently accompanied by vomiting. Finally in the fall of 1946 the patient had a particularly severe attack and was admitted to the wards of the Hopkins Hospital, intussusception having been first suspected. At operation a very large intussusception of ileum into colon as far as the transverse colon was found. Some 2 feet of ileum and the colon as far as the mid-transverse portion was removed. Two polyps presumably cause of the trouble were found in the ileum portion of the specimen. Six months after that admission in [REDACTED] 1947 the patient began to have dizziness and s.o.b. on severe exertion. Examination then revealed a severe microcytic hypochromic anemia with a Hgb. of 4.0 grams, a MCV of 56, MCHC of 23. Stools were consistently positive for occult blood. However since it was impossible to localize the polyps he was believed almost certainly to have no further surgery was done at that time. Ferrous sulfate and transfusion returned the blood picture to normal. In [REDACTED] 1948 the patient was again admitted for intussusception. Two groups of polyps were felt in the jejunum and these portions of the intestine resected.

In 1946 it was first noted that this boy has a peculiar pigmentary anomaly. The spotting of the outside of the lips is quite apparent from this photograph. This photograph shows more of the lip spots and also the spots on the buccal mucosa. And here are the spots on the digits. This spot on the palm was biopsied. Incidentally in this patient no family history of intestinal trouble or this pigmentary anomaly could be elicited. This is the only person with negro blood and the syndrome. In 1947 the second of these cases came to my attention. This was a 15 year old girl from South Carolina. There had been one previous Hopkins Hospital admission at the age of 6 years, because of anemia, full abd. pain with occasional severe attacks and run-down condition for 18 months.

The pigmentary anomaly was described then but its diagnostic significance not appreciated. The admission diagnosis was Meckel's diverticulum. While in the hospital the intussusception and at operation two ilee-ileal intussusceptions and a total of 3 large polyps were found. Thereafter the patient did well until 1946 when she began to lose weight, felt weak much of the time and finally in the summer of 1947 her old crampy abd. pain returned. She was thoroughly explored in [REDACTED] 1947. Two polyps were found in the stomach. These were removed by elliptical resection. Others were palpated in distal jejunum and proximal ileum and four feet of this part of the gut was resected. Eight large polyps were found in it. The patient has done very well since that time in spite of the fact that it was thought that polyps could be felt in the transverse colon at operation.

This picture shows the spots of the outside of the lips, and the next two are the spots of the buccal mucosa. Again in this case no family history of intestinal trouble or pigmentary anomaly can be elicited.

The next three cases of this syndrome are members of the same family. In the spring of 1948 Dr. Mark Ranitch, a local surgeon, was speaking to the Harrisburg, Pa., Medical Society on intussusception and mentioned this syndrome in which we had been interested. After his talk Dr. Clarence Moore a Harrisburg surgeon told Dr. Ranitch he had operated on three members of one family for intussusception due to small intestinal polyps, that all three had spots on their lips, and that he would be happy for me to study these cases. I went to Harrisburg soon thereafter. Dr. Moore had the three patients come in to his office, I studied the operative notes and histologic sections, and I examined the patients and got photographs of them. This is the only one I have a lantern slide of. This patient had had almost daily "bellyaches" from an early age and finally was operated on by Dr. Moore at the age of 18, at age of 22 and at age of 27 for acute intussusceptions. Each time sections of small intestine containing polyps being removed.

A sister of this patient began to have crampy abdominal pain in her teens and was operated on at age 16 with discovery of polyps in the jejunum, a segment of which was removed.

And a brother of these two patients had abdominal pain esp. after eating begin at age of 20. At age 22 he was operated on for intussusception with discovery of polyps of the jejunum.

The spotting in these three cases was almost identical and this picture serves to demonstrate the degree of pigmentation in this family.

At the time I examined these patients a brother and sister were said to have no pigmentary anomaly and to be free of abd. complaints. However, in [REDACTED] of this year the female patient wrote that the younger brother, 22 yr. old while away at work had been seized with an acute abdominal attack, had been operated on as acute appendicitis, but found to have intussusception due to polyps for which resection was done. However, the patient died 2 days following operation due to unclear causes. The patient's family as far as they can recall do not believe this patient had the characteristic spots.

Dr. Harold Leghus formerly of Boston City Hospital, now Professor of Medicine at Georgetown, likewise has collected 75 cases of the syndrome. This is one of his cases; a white girl who died at age 14. At the age of 8 she was twice operated on for intussusception. Thereafter she had frequent bouts of diarrhea. She succumbed to pneumonia. Autopsy revealed polyps in the stomach, the entire length of what remained of the small intestine, and a single one in the sigmoid colon.

This picture shows mother and daughter both of whom had the full syndrome. The mother began to have increasing constipations at the age of 39, began to have increasing constipation together with intermittent rectal bleeding and later rectal prolapse with protrusion of mass. A series of operations was embarked upon: ileostomy, partial colectomy, fulguration of rectosigmoid polyps, etc. The patient developed numerous rectal fistulas, multiple peritoneal abscesses and finally died within a year of first symptoms. At autopsy the stomach, duodenum, jejunum, ileum, and rectum all contained polyps.

This picture shows mother and daughter both of whom had the full syndrome. The mother was a cousin of the patient whose picture you just saw. The brother had a 10 yr. history of intermittent abd. attacks. Appendectomy was done during one such attack. At age 30 she was operated on for intussusception of the ileum due to polyps. At the time of last follow-up she had had no recurrence of symptoms.

The daughter at age 7 began to have recurrent attacks of severe crampy abd. pain localized at the umbilicus. At age 9 she was admitted to the Boston Children's Hospital in a severe attack of this description and a laparotomy was found to have a jejunoileal intussusception. Postoperatively she developed pneumonia, empyema and peritonitis and died. At autopsy the stomach, entire small intestine and rectum showed polyps.

This is the picture of a case of the syndrome which was sent us by Dr. Francesco Ronchese of Provident. Ronchese is a very wide-awake dermatologist who is perhaps best known for his publications on occupational stigmata. This was a 21 yr. old white girl who before she was first admitted to the Providence Hospital had had intermittent abd. pain consistent with intussusception for 3 mos. On laparotomy during such an attack intussusception of terminal ileum into the colon was found. The polypoid growth causing the intussusception was said to be adeno-carcinoma histologically. I think this is dubious. Four years after this first operation symptoms recurred, and laparotomy with removal of polyps from both stomach and ileum were performed. To date the patient has done well.

In addition to these 10 cases Dr. Leghus and I have seen 3 other cases during the past summer. One was picked up at the Bethesda Naval Hospital by one of Dr. Leghus' students who is interning there. Two others were recognized at the Pratt Diagnostic Hospital in Boston within a few months of each other. All three of these cases have the full syndrome, i.e. frequent intussusceptions and chronic anemia from G.I. bleeding in addition to spots. This shows the spotting of the hands in this case.

On the basis of these thirteen or fourteen cases we are attempting to nail down a syndrome never before described as such in the English literature. In fact influences in the continental literature as well is quite scanty and, I fear, unconvincing.

It has taken us 3 years to search the literature in a detailed fashion for references to the association of polyps and spots. It has taken so long mainly because references to the association are for the most part buried as mere notes deep in the voluminous surgical literature on polyposis or the equally voluminous dermatologic literature on pigmentary anomalies. By supplementing the publications we found with communications from the authors we have accumulated a total of 21 cases, proven, probable, or possible in addition to our own cases.

It was Dr. Chester Keefer who after seeing some of our cases, recalled that the pigmentary part of this syndrome was described as an isolated curiosity by Sir Jonathan Hutchinson of Hutchinson triad fame in his Archives of Surgery for 1896. Dr. Keefer is a medical bibliophile, has a very valuable collection of pre-1900 medical literature, among these books Hutchinson's Archives. Hutchinson was a fascinating character. I wish there were time to dilate on his biography. His Archives of Surgery was an annual affair to which he was the sole contributor. The wealth of clinical material beautifully illustrated with colored plates is fabulous. I came across these remarks of Sir William Oster in eulogizing Hutchinson. They seem appropriate in this particular situation.

"When anything turns up which is anomalous or peculiar, anything upon which the textbooks are silent and the systems and cyclopaedias are dumb, I tell my students to turn to the volumes of Mr. Hutchinson's Archives of Surgery, since if it is not mentioned in them, we are surely dealing with something very much out of the common."

Sarcoid, temporal arteritis, lupus erythematosus disseminatus are but a few of the conditions he describes in detail.

This is a copy of the colored plate which Hutchinson published in 1896 showing twelve yr. old twins with the exact pigment anomaly I have shown so many examples of this morning. Hutchinson did not know about any polyposis for he wrote: "That they (referring to the spots) are not in any active sense pathological we may safely assume for they appear to be not aggressive, and their subjects remain in perfect health."

In 1919 F. Parkes Weber published a follow-up on Hutchinson's twins. Altho one was living and well one had died at the age of 20 of intussusception. F. Parkes Weber is an interesting character too, a syndrome describer from way back. It was he who described Weber-Sturges syndrome, Weber-Christian's disease and a number of other conditions that bear his name. Dr. Weber is still living at age 86, in fact still sees patients in his consulting rooms at #13 Harley St. in London. I wrote to Dr. Weber and in his letter of reply he stated that the father of the twins was a [REDACTED], that a son had succeeded him in that work. He obtained for me a

copy of the death certificate of the twin who had died of intussusception at age 20. It seems almost certain that twin had polyps since at age 20 one doesn't ordinarily get intussusception without polyps or carcinoma.

Dr. Forman, dermatologist at Guy's Hospital visited Hopkins in 1947 and saw the colored boy with syndrome who I showed you first. He very kindly tracked down [REDACTED] brother of the twins and got from him the story that the second twin had died of carcinoma of the breast at the age of 58, that no other members of the family have had either the pigment anomaly or intestinal troubles.

The next reference to the syndrome is an obscure Dutch journal by Pentz an internist of the Hague in 1921. He published a family in which several members were involved. He describes 4 in his original publication. Dr. Pentz was kind enough to send me further observations on this same family in which he has found 7 cases of the full syndrome. I show these photographs which Dr. Pentz sent me of mother and son with the syndrome to show how very extensively the face may be involved.

Under the title "Adenocarcinoma of the Small Intestine in Father and Daughter", Foster of the Llandough Hospital in Cardiff, Wales, described in 1935 father and dau. who within a few mos. of each other developed intussusception due to polypoid tumors in the jejunum diagnosed adeno ca. by his pathologist. He makes the remark that both had spotting of the lips but he published no photographs. This is a photograph of the daughter he was good enough to send me together with other follow-up material.

In 1946 in the Presse Medicale Touraine a dermatologist in Paris published a case of the full syndrome. This is his case. This is the inside of the mouth in his case.

There are other scattered reports. One for instance from and by a Dutch surgeon of Indonesian sisters with the full syndrome.

This slide demonstrates several things; (1) These people get into trouble from their polyps in their teens or twenties.

(2) There is a slight predominance of females in the 10 cases we have studied in detail.

(3) There is a wide ethnologic spread. One of our cases was negro. Cases have been described in Frenchmen, Dutchmen, Welsh, Englishmen, and Indonesians.

(4) About half the cases have family histories.

(5) There is occasional malignant degeneration.

(6) Polyps of the small intestine are invariable.

The polyps of this syndrome are in no way distinctive histologically.

This slide shows significant characteristics of the pigmentation. Evolvment of the mouth and lips is a sine qua non. All these patients are of dark complexion.

The histology of these spots based on biopsy in my negro pt. is very interesting. The pigment deposits occur in bands traversing all layers of

of the epidermis. This is particularly interesting since we have observed that when the melanin spots are examined with a magnifying glass one gets an impression of stippling.

We have sufficiently complete geneologic data on 4 families to permit construction of family trees. This is the chart of the Harrisburg family, Boston family, the Welch family and the Dutch family.

This slide gives the genetic characteristics.

In addition to the fact that some cases in these families have only spots this last statement is based on a case I saw in the POPC at Hopkins 1½ yr. ago. The patient was a 50 yr. old woman from Mexico City. She had spots which appear to have all the characteristics of those seen in this syndrome. However, we could obtain no history of intestinal complaints nor any radiographic or sigmoidoscopic evidence of polyps.

I wanted to call this syndrome to the attention of this group since it cuts across the interest of several fields, that of the gastroenterologist, the dermatologist, the surgeon, the oncologist, the dentist, etc.